REMARKS

The Restriction Requirement

The pending claims, claims 1-42, are subject to a restriction requirement in which the claims were assigned to 54 different groups. Applicants submit that the restriction requirement is in error and should be modified as follows.

Request for Reconsideration

Applicants submit that Groups I, X, XIII, XLIII, XLVI, and XLIX should be examined together. The claims of Groups I, X, XIII, XLIII, XLVI, and XLIX are linked by a common, inventive concept, as is discussed below, namely a purified antibody that preferentially binds to a CDR3-loop of a TCR and methods of making and using the purified antibody. Applicants respectfully submit that examining the claims of Groups I, X, XIII, XLIII, XLVI, and XLIX together would not present an undue burden on the Examiner. Thus, Applicants respectfully request that the restriction requirement be modified to combine Groups I, X, XIII, XLIII, XLVI, and XLIX into one group.

Group I (claims 1-5 and 7) contains claims directed to a purified antibody, a hybridoma that produces an antibody, and a combination of purified antibodies that preferentially binds a CDR3-loop of a T cell antigen receptor (TCR). Group X (claims 9 and 11) contains claims that, as amended in the Preliminary Amendment enclosed herewith, are directed to a method of generating the antibody of claim 1 by immunizing a

mammal with coupled peptides. Group XIII (claims 10 and 11) contains claims that, as amended in the Preliminary Amendment enclosed herewith, depend from claim 9 and are directed to an antibody of claim 9 generated by a method that includes immunizing a mammal with coupled peptides and with invariant T cells. Group XLIII (claim 23-30) contains claims that are directed to a method of increasing the size of a subpopulation of T cells by contacting a sample that includes the T cells with an antibody or combination of antibodies of claim 1; the method can be performed in the presence or absence of α-galactosylceramide. Group XLVI (claims 31 and 32) contains claims that are directed to a method of increasing the size of a subpopulation of T cells in a mammal by contacting the T cells with an antibody or combination of antibodies of claim 1 under conditions that allow the contacting to increase the number of T cells and administering the T cells to the mammal. Group XLIX (claims 33-38) are directed to a method of increasing the size of a subpopulation of T cells in a mammal by contacting the T cells with an antibody or combination of antibodies of claim 1, under conditions that allow complex formation between the T cells and the antibody, in the presence or absence of α-galatosylceramide, and administering the T cells to the mammal.

As is clear from the brief description above of the subject matter of the claims of Groups I, X, XIII, XLIII, XLVI, and XLIX, the common, inventive concept that links these restriction Groups is a purified antibody that preferentially binds to a CDR3-loop of a TCR and methods of making and using the purified antibody. Applicants respectfully

request that the restriction requirement be modified to combine Groups I, X, XIII, XLIII, XLVI, and XLIX into one group. In accordance with the Examiner's requirement that Applicants elect a species for the method of group XLIX, Applicants elect autoimmune disease.

If the Examiner disagrees with the combination of Groups I, X, XIII, XLIII, XLVI, and XLIX, Applicants respectfully request that the Examiner alternatively consider modifying the restriction requirement to rejoin either the claims of Groups I, X, and XIII into a single restriction group or the claims of Groups I, XLIII, XLVI, and XLIX into a single restriction group. Given a choice between one of these two alternative restriction groups, Applicants would preferentially elect the claims of rejoined Groups I, X, and XIII. For the reasons discussed below, Applicants submit that the claims of each of the alternative restriction groups are linked by a common, inventive concept, and it would not be an undue burden on the Examiner to examine the claims of either of these two alternative restriction groups together in one application.

Groups I, X, and XIII

Claims 9-11 (groups X and XIII) are directed to processes for making the antibody of claim 1. Applicants respectfully assert that it would not be unduly burdensome for the claims of Examiner's Groups I, X, and XIII to be examined in one application.

As an initial matter, claim 10, as amended in the accompanying Preliminary

Amendment, now depends from claim 9, because, as described in the specification at page 9, line 14, through page 11, line 3, the methods for making the antibody that include the use of a cyclic peptide and the methods that include the use of invariant T cells to immunize the animal are not mutually exclusive and can be used together. At page 52, line 14, through page 53, line 8, the specification describes the generation of antibodies as follows.

> Because all invariant TCR^+ T cells from all individuals have the same amino acid sequence in the CDR3 loop, this region was used in the design of peptides for the generation of anti-CDR3-loop antibodies. Because the murine and human sequence of the CDR3 loop are nearly identical (CVVSDRGST and CVVGDRGSA; SEQ ID NOs 2 and 3, respectively), a peptide with the human CDR3 loop sequence that is administered to mice might be recognized by the murine immune system as a self peptide and thus not induce the production of antibodies.
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> To overcome this potential problem, CD1d knockout mice (Sonoda *et al.*, supra) which lack invariant TCR^+ T cells were used as the host for the production of anti-CDR3-loop antibodies. Since these mice lack the invariant TCR- α chain they are able to recognize peptides containing the human CDR3 loop sequence as foreign, and thus, generate antibodies against this epitope....Invariant TCR^+ T cells were later administered to some mice to further stimulate the immune system.

As is clearly described in the specification, the methods as recited in claims 9 and 10 as filed are not mutually exclusive and can be used together.

Applicants submit that the method of Examiner's Groups X and XIII, as amended in the enclosed Preliminary Amendment, cannot be practiced with a materially different product than the antibodies of Examiner's Group I and should therefore be examined together. Applicants also submit that the same literature search can be used to examine

claims directed to the antibodies and to the methods of methods of making the antibodies. Thus, it would not be an undue burden on the Examiner to evaluate the antibodies and the methods of making the antibodies in a single restriction group that includes the claims of Groups I, X, and XIII. *See* MPEP § 803. Accordingly, Applicants respectfully request that the restriction requirement be modified to combine the claims of Groups I, X, and XIII into one restriction group. In the alternative, if the Examiner finds the combination of Groups I, X, and XIII to be inappropriate, Applicants respectfully request that the restriction requirement be modified to rejoin at least the claims of Groups I and X, which are directed to the product and the method of making the product.

Groups I, XLIII, XLVI, and XLIX

Groups XLIII, XLVI, and XLIX are all directed to methods of using a purified antibody or combination of antibodies that preferentially binds to a CDR3-loop of a TCR. As presently amended, the claims of these groups are directed to a method that includes contacting either a sample that includes T cells or the T cells themselves with an antibody or combination of antibodies of claim 1.

According to MPEP § 808,

> Every requirement to restrict has two aspects: (A) the reasons (as distinguished from the mere statement of conclusion) why each invention *as claimed* is either independent or distinct from the other(s); and (B) the reasons why there would be a serious burden on the examiner if restriction is not required....

With respect to point (A), Applicants submit that, in view of the present amendment to claims 23, 27, 29, 31, 33, and 35, the claims of restriction Groups XLIII, XLVI, and XLIX are not independent or patentably distinct from the claims of restriction Group I, because they all depend from claim 1 and are joined by the same inventive concept, namely the use of an antibody of combination of antibodies of claim 1 to increase the size of a subpopulation of T cells. With respect to point (B), Applicants submit that searching the subject matter of the claims of Groups XLIII, XLVI, and XLIX together would not pose an undue burden and this submission is supported by the fact that the Examiner has classified each of these groups into the same class (Class 424) and subclass (Subclass 178.1). Further, the Examiner has not provided a showing that the claims have a separate status in the art or have a different field of search, as provided by MPEP § 808.02. Accordingly, Applicants respectfully request modification of the restriction requirement to rejoin the claims of Groups XLIII, XLVI, and XLIX into a single restriction group and to further combine Groups XLIII, XLVI, and XLIX with Group I. In the alternative, if the Examiner finds the combination of Groups XLIII, XLVI, and XLIX to be inappropriate, Applicants respectfully request that the restriction requirement be modified to rejoin at least the claims of Groups I and XLIII as the product and the method of using the product.

In summary, given that each of the claims in Groups I, X, XIII, XLIII, XLVI, and

XLIX involves an antibody that binds to a CDR3-loop of a TCR and methods of making the antibody or using the antibody to increase the size of a subpopulation of T cells, examining these six restriction groups together would not present an undue burden on the Examiner. For the reasons set forth above, Applicants request that the restriction requirement be modified to combine Groups I, X, XIII, XLIII, XLVI, and XLIX into one group.

In the alternative, Applicants respectfully request that at least the claims of Groups I, X, and XIII or the claims of Groups I, XLIII, XLVI, and XLIX be rejoined. Given a choice between one of these two alternative restriction groups, Applicants would elect to proceed with examination of the claims of Groups I, X, and XIII.

Applicants have also amended the claims of the present application, submitted herewith in the enclosed Preliminary Amendment, to conform with this election and the arguments presented herein.

CONCLUSION

Enclosed is a petition to extend the period for replying for two months, to and including December 28, 2005, and a check for the required fee under 37 C.F.R. § 1.17(a). Also enclosed is a check in payment of the excess claims fee.

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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